Amyloid Myopathy: A Challenging & Delayed Diagnosis

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Introduction

Amyloidosis is a challenging diagnosis due to several confounding factors including multi-organ involvement, variable presentations of disease and difficulty in obtaining a timely diagnosis due to availability of histopathologic stains.

Case Presentation

HPI:

A 70-year-old male was referred to hematology for evaluation of progressive bilateral weakness and abnormal labs.

Past Medical History

Mitral valve endocarditis s/p mechanical MVR and splenectomy in 1996
Persistent atrial fibrillation s/p atrioventricular nodal ablation and pacemaker in 1998, on dofetilide,
HFrEF (EF 30-35%)

Physical Exam

End systolic murmur 2/6 over RUSB. Mechanical S2 click.
JVP 4cm at 90 degrees. Bilateral 2+ pitting edema to the thighs.
Wheelchair dependent; CN's II-XII intact
No reflexes bilaterally (biceps, triceps, patellar, achilles)
Sensation to light touch, vibration, proprioception intact
Severe asymmetric proximal greater than distal weakness
RLE weakness >LLE weakness; LUE weakness >RUE weakness

Laboratory data

ANA + 1:80 titers
ANCA panel, RNP, anti-Smith, anti scleroderma,
Anti SS-A/SS-B, Anti Jo-1 negative
CK: 294 (49-397)
Serum MMA: 689 nmol/L (0-378)
LDH: 515U/L (<250U/L)
Free Kappa Lt chain 22.2mg/L (3.3-19.4)
Free Lambda Lt chains 716.5mg/L (5.7-26.3)
Kappa/Lambda Ratio: 0.03 (0.26-1.65)

Clinical Course & Follow Up

03/2019: Mobility issues, newly walker dependent, diagnosed with severe L knee osteoarthritis.

06/2019: Underwent Left total knee arthroplasty. Discharged to SNF for rehab.

06/2020: PCP appointment for 2 GLF after failure to graduate SNF x 1 year. CT with degenerative changes, foraminal narrowing in cervical spine. Not enough to explain symptoms.

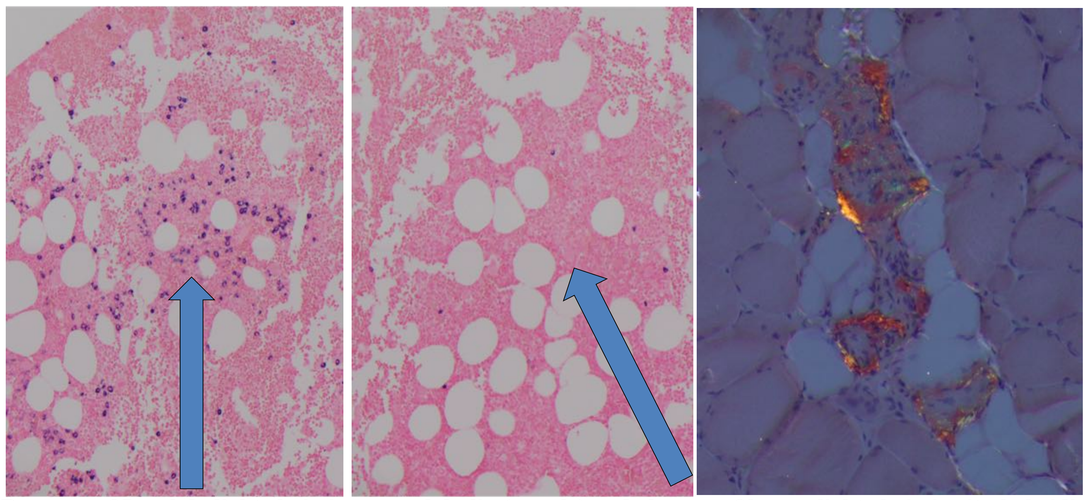
12/2020: EMG with distal muscles chronic denervation; proximal LE muscles acute denervation. Neuropathy workup with abnormal FLC.

03/2021: Hematology Evaluation, now wheelchair dependent. Concern for myeloma. Bone Marrow Biopsy with 15% clonal plasma cell, lambda light chain restricted.

04/2021: Diagnosed with AL amyloidoisis with primarily muscle involvement (confirmed on biceps biopsy) and stage IIIA cardiac amyloid (elevated troponins and NT-ProBNP)

06/2021: 2 cycles of daratumumab, cyclophosphamide, bortezomib and dexamethasone but course was complicated by acute renal failure, when he transitioned to hospice and died.

Imaging



Presence of Lambda light chain immunoglobulin (purple) and absence of kappa light chain in situ hybridization (center) on section of bone marrow biopsy with amyloid seen on Congo Red staining on muscle biopsy (right)

Discussion

- Amyloid affects 12,000 people nationally[1], prevalence rising
- Initial symptoms are non-specific-fatigue, lightheadedness and weight loss. Heart and Kidneys are most commonly affected organs with heart failure, edema and proteinuria[2]
- Amyloid Myopathy seen in **1.5%** of patients with amyloid[3]
  - **Rarely presents as initial symptom**
- Screening for Amyloid Myopathy includes evaluation of **Monoclonal Gammopathy with SPEP, FLC and muscle biopsy - critical** for diagnosis[3].
  - Congo Red staining **not** usually sent on biopsies
- CK usually **normal** in most patients, ESR/CRP are nonspecific.
- AL amyloidosis **responds to chemotherapy** but is often diagnosed too late in the disease course[4,5]

References

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